## REMARKS

Claims 1-4 are pending in the instant application. Claims 1-4 have been rejected. Claims 1 and 2 have been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

### I. Withdrawn Objections

Applicant is pleased to acknowledge that the objection to the drawings; rejection of claims 1-4 under 35 U.S.C. §112, first paragraph; rejection of claims 2 and 4 under 35 U.S.C. §112, second paragraph; and rejection of claims 1 and 4 under 35 U.S.C. §102(a) as being anticipated by Melhuish and Wotton (December 2000, *J. Biol. Chem.* 275(50):39762-39766) have all been withdrawn.

### II. Rejection of Claims Under 35 U.S.C. §112

Claims 1-4 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not disclosed in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner suggests that there is no support in the specification for narrowing the scope of the claims to include a Smad protein co-repressor in the complex or limiting the co-repressor to a Smad protein co-repressor. The Examiner further suggests that this section of the specification does not support the contemplation of such a complex in the manner set forth in claim 1.

Applicant respectfully traverses this rejection.

Applicant believes that the specification, when taken as a whole, clearly describes a complex inclusive of a Smad protein, a Smad protein co-repressor and a CtBP protein. For example, see page 7, lines 12-19 which recites that "screening and testing methods are based on the finding that the Drosophila Smad proteins, Mad and Medea, are able to interact directly with the co-repressor protein CtBP through the Smad MH1 domain. This was unexpected since the MH1 domain of these Smad proteins is known to lack a CtBP interaction motif or binding site. A Drosophila DNA-binding Smad co-repressor, Schnurri, has also been shown to interact both with Mad and with CtBP." [Emphasis added]. Further, page 8, lines 20-22 recites that "It has now been found that Smad proteins cooperate with DNA-bound co-repressor, Schnurri, to recruit a second co-repressor called CtBP", thereby indicating that these three proteins interact to form a complex. Moreover, page 14, lines 11-21 of the specification specifically contemplates protein interactions and complex formation in the recitation "assays can be developed, for example to identify proteins or small molecules that interact with Smad proteins to prevent interactions of CtBP with Smads or with DNA-binding co-repressors (e.g., Evi-1, TGIF, SIP1 or Schnurri), or formation of a DNA-bound complex containing Smads, CtBP and DNA-binding co-repressors, and thus prevent repression of genes that are negatively regulated by TGFβ signaling pathways, or to identify and clone genes that are directly or negatively regulated by TGF-β signaling pathways."

In an effort to further the prosecution of this application, Applicant has further amended claims 1 and 2 to clarify the assay of the invention. Claim 1 and 2 now recite that the assays of the

present invention utilize cells containing the interacting proteins comprising a Smad protein, a Smad protein co-repressor and a CtBP protein. This is novel in the art as the present invention discloses that these proteins have not been previously shown to interact (see, *e.g.*, page 8, lines 20-22). Withdrawal of this rejection is therefore respectfully requested.

**III. Conclusion**

The Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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